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 NEWS  3  OCT 23   The Derwent World Patents Index suite of databases on STN
                   has been enhanced and reloaded
 NEWS  4  OCT 30   CHEMLIST enhanced with new search and display field
 NEWS  5  NOV 03   JAPIO enhanced with IPC 8 features and functionality
 NEWS  6  NOV 10   CA/CAplus F-Term thesaurus enhanced
 NEWS  7  NOV 10   STN Express with Discover! free maintenance release Version
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 NEWS  8  NOV 20   CA/CAplus to MARPAT accession number crossover limit increased
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 NEWS  9  DEC 01   CAS REGISTRY updated with new ambiguity codes
 NEWS 10  DEC 11   CAS REGISTRY chemical nomenclature enhanced
 NEWS 11  DEC 14   WPIDS/WPINDEX/WPIX manual codes updated
 NEWS 12  DEC 14   GBFULL and FRFULL enhanced with IPC 8 features and
                   functionality
 NEWS 13  DEC 18   CA/CAplus pre-1967 chemical substance index entries enhanced
                   with preparation role
 NEWS 14  DEC 18   CA/CAplus patent kind codes updated
 NEWS 15  DEC 18   MARPAT to CA/CAplus accession number crossover limit increased
                   to 50,000
 NEWS 16  DEC 18   MEDLINE updated in preparation for 2007 reload
 NEWS 17  DEC 27   CA/CAplus enhanced with more pre-1907 records
 NEWS 18  JAN 08   CHEMLIST enhanced with New Zealand Inventory of Chemicals
 NEWS 19  JAN 16   CA/CAplus Company Name Thesaurus enhanced and reloaded
 NEWS 20  JAN 16   IPC version 2007.01 thesaurus available on STN
 NEWS 21  JAN 16   WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
 NEWS 22  JAN 22   CA/CAplus updated with revised CAS roles
 NEWS 23  JAN 22   CA/CAplus enhanced with patent applications from India
 NEWS 24  JAN 29   PHAR reloaded with new search and display fields
 NEWS 25  JAN 29   CAS Registry Number crossover limit increased to 300,000 in
                   multiple databases

 NEWS EXPRESS  NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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=> s (brain(w)tumor) and (GnRH or gonadotropin(w)releasing(w)hormone or luteinizing(w)hormone(w)releasing(w)hormone or LHRH)
L1 81 (BRAIN(W) TUMOR) AND (GNRH OR GONADOTROPIN(W) RELEASING(W) HORMONE OR LUTEINIZING(W) HORMONE(W) RELEASING(W) HORMONE OR LHRH)

=> s l1 and treatment
L2 44 L1 AND TREATMENT

=> dup rem l1
PROCESSING COMPLETED FOR L1
L3 44 DUP REM L1 (37 DUPLICATES REMOVED)

=> dup rem l2
PROCESSING COMPLETED FOR L2
L4 24 DUP REM L2 (20 DUPLICATES REMOVED)

=> dis ibib abs l4 1-24

L4 ANSWER 1 OF 24 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2006381380 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16624606
TITLE: Pathophysiology of radiation-induced growth hormone deficiency: efficacy and safety of GH replacement.
AUTHOR: Darzy Ken H; Shalet Stephen M
CORPORATE SOURCE: Department of Endocrinology, Christie Hospital NHS Trust, Wilmslow Road, Withington, Manchester M20 4BX, United Kingdom.
SOURCE: Growth hormone & IGF research : official journal of the Growth Hormone Research Society and the International IGF Research Society, (2006 Jul) Vol. 16 Suppl A, pp. S30-40. Electronic Publication: 2006-04-18. Ref: 109
Journal code: 9814320. ISSN: 1096-6374.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200612
ENTRY DATE: Entered STN: 27 Jun 2006

Last Updated on STN: 19 Dec 2006
Entered Medline: 7 Dec 2006

AB Radiation-induced growth hormone deficiency (GHD) is primarily due to hypothalamic damage. GH secretion by the pituitary may be affected either secondary to some degree of quantitative deprivation of hypothalamic input or, if the radiation dose is high enough, by direct pituitary damage. As a consequence, the neurosecretory profile of GH secretion in an irradiated patient remains pulsatile and qualitatively intact. The frequency of pulse generation is unaffected, but the amplitude of the GH pulses is markedly reduced. Over the last 25 years, the final heights achieved by children receiving GH replacement for radiation-induced GHD have improved; these improvements are attributable to refinements in GH dosing schedules, increased use of GnRH analogues for radiation-induced precocious puberty, and a reduced time interval between completion of irradiation and initiation of GH therapy. When retested at the completion of growth, 80-90% of these teenagers are likely to prove severely GH deficient and, therefore, will potentially benefit from GH replacement in adult life. Such long-term GH treatment in patients treated previously for a brain tumor means that critical and continuous surveillance must be devoted to the risk of tumor recurrence and the possibility of second neoplasms.

L4 ANSWER 2 OF 24 EMBASE

ACCESSION NUMBER: 2005137130 EMBASE
TITLE: Targeting cytotoxic conjugates of somatostatin, luteinizing hormone-releasing hormone and bombesin to cancers expressing their receptors: A "smarter" chemotherapy.
AUTHOR: Nagy A.; Schally A.V.
CORPORATE SOURCE: A. Nagy, Section of Experimental Medicine, Department of Medicine, Tulane University School of Medicine, New Orleans, LA 700112, United States. dcallai@tulane.edu
SOURCE: Current Pharmaceutical Design, (2005) Vol. 11, No. 9, pp. 1167-1180. .
Refs: 108
ISSN: 1381-6128 CODEN: CPDEFP
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
016 Cancer
030 Pharmacology
037 Drug Literature Index
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 14 Apr 2005
Last Updated on STN: 14 Apr 2005

AB Chemotherapy is one of the main modalities in the therapy of cancer. However, an improvement in the efficacy and a reduction in the toxicity of chemotherapeutic agents remains a great challenge to oncologists. A specific delivery of cytotoxic drugs to cancerous cells may help improving both aspects. Peptide hormones, for which receptors have been found in various human cancers, can serve as carriers for a local delivery of cytotoxic agents or radiopharmaceuticals to the tumors, as demonstrated by the successful clinical use of radiolabeled somatostatin analog Octreoscan for the detection and treatment of some somatostatin receptor-positive tumors. Thus, in recent years we developed a series of cytotoxic peptide hormone conjugates based on derivatives of hypothalamic hormones such as somatostatin and luteinizing hormone-releasing hormone (LHRH), and the brain-gut hormone bombesin. To create targeted conjugates with high cytotoxic activity, a derivative of doxorubicin (DOX), 2-pyrrolino-DOX (AN-201), which is 500-1, 000 times more active than its parent compound, was

developed. This agent was coupled to somatostatin octapeptide RC-121 to form cytotoxic conjugate AN-238, and to [D-Lys(6)]LHRH carrier to produce analog AN-207. Cytotoxic bombesin hybrid AN-215 also contains AN-201. DOX was likewise linked to [D-Lys(6)]LHRH to form AN-152. A comprehensive testing of these cytotoxic conjugates in experimental models of various human and rodent cancers led to their selection as candidates for clinical trials. .COPYRGT. 2005 Bentham Science Publishers Ltd.

L4 ANSWER 3 OF 24 MEDLINE on STN
ACCESSION NUMBER: 2005121389 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15751842
TITLE: [New approaches to treatment of various cancers based on cytotoxic analogs of LHRH, somatostatin and bombesin].
La quimioterapia dirigida. nuevas modalidades para el tratamiento de varios canceres con analogos cititoxicos de LH-RH, somatostatina y bombesina.
AUTHOR: Schally Andrew V
SOURCE: Anales de la Real Academia Nacional de Medicina, (2004) Vol. 121, No. 3, pp. 493-500.
Journal code: 7505188. ISSN: 0034-0634.
PUB. COUNTRY: Spain
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Spanish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200510
ENTRY DATE: Entered STN: 9 Mar 2005
Last Updated on STN: 18 Oct 2005
Entered Medline: 17 Oct 2005

AB The development of targeted cytotoxic analogs of hypothalamic peptides for the therapy of various cancers is reviewed and various oncological studies on experimental tumors are summarized. Novel therapeutic modalities for breast, prostate and ovarian cancer consist of the use of targeted cytotoxic analogs of LH-RH containing doxorubicin (DOX) or 2-pyrrolino-DOX. The same radicals have been incorporated finto cytotoxic analogs of somatostatin which can be also targeted to receptors for this peptide in prostatic, mammary, ovarian, renal cancers, brain tumors and their metastases, A targeted cytotoxic analog of bombesin containing 2-pyrrolino-DOX has been also synthesized and successfully tried in experimental models of prostate cancer, small cell lung carcinoma and brain tumors. The development of these new classes of peptide analogs should lead to a more effective treatment for various cancers.

L4 ANSWER 4 OF 24 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004444443 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15350601
TITLE: Chemotherapy targeted to cancers through tumoral hormone receptors.
AUTHOR: Schally Andrew V; Nagy Attila
CORPORATE SOURCE: Endocrine, Polypeptide and Cancer Institute, Veterans Affairs Medical Center and Department of Medicine, Tulane University School of Medicine, New Orleans, LA 70112, USA.. dcallai@tulane.edu
SOURCE: Trends in endocrinology and metabolism: TEM, (2004 Sep) Vol. 15, No. 7, pp. 300-10. Ref: 76
Journal code: 9001516. ISSN: 1043-2760.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502

ENTRY DATE: Entered STN: 8 Sep 2004
Last Updated on STN: 8 Feb 2005
Entered Medline: 7 Feb 2005

AB Work on cytotoxic analogs of luteinizing hormone-releasing hormone (LH-RH), somatostatin and bombesin, designed for targeting chemotherapy to peptide receptors on various cancers, is reviewed here as the project is at advanced stages of development and clinical trials are pending. Cytotoxic analogs of LH-RH, AN-152 and AN-207, containing doxorubicin (DOX) or 2-pyrrolino-DOX (AN-201), respectively, target LH-RH receptors and can be used for the treatment of prostatic, breast, ovarian and endometrial cancers and melanomas. AN-201 was also incorporated into the cytotoxic analog of somatostatin, AN-238, which can be targeted to receptors for somatostatin in prostatic, renal, mammary, ovarian, gastric, colorectal and pancreatic cancers as well as glioblastomas and lung cancers, suppressing the growth of these tumors and their metastases. A cytotoxic analog of bombesin AN-215, containing 2-pyrrolino-DOX, was likewise synthesized and successfully tested in experimental models of prostate cancer, small cell lung carcinoma, gastrointestinal cancers and brain tumors expressing receptors for bombesin/gastrin-releasing peptide. This new class of targeted cytotoxic peptide analogs might provide a more effective therapy for various cancers.

L4 ANSWER 5 OF 24 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:347965 BIOSIS
DOCUMENT NUMBER: PREV200510141065
TITLE: 17th Annual Meeting of the Sociedad-Latinoamericana-fe-Endocrinologia-Pediatrica, Angra dos Reis, BRAZIL, October 24 -28, 2004.
AUTHOR(S): Anonymous
SOURCE: Journal of Pediatric Endocrinology & Metabolism, (OCT 2004) Vol. 17, No. Suppl. 5.
Meeting Info.: 17th Annual Meeting of the Sociedad-Latinoamericana-fe-Endocrinologia-Pediatrica. Angra dos Reis, BRAZIL. October 24 -28, 2004. Soc Latin Amer Endocrinol Pediat.
CODEN: JPENEV. ISSN: 0334-018X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Summary)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Sep 2005
Last Updated on STN: 8 Sep 2005

AB This meeting contains 30 oral presentations, 14 miniposter presentations, and 72 poster presentations written in English on endocrinology and metabolism. Diseases discussed include but are not limited to precocious puberty, insulin resistance syndrome, brain tumor, obesity and dyslipidemia. Disease prognosis, drug therapy, disease-free survival, chronological age, and anthropometric indicators are also discussed.

L4 ANSWER 6 OF 24 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2003379636 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12915655
TITLE: Improvements in final height over 25 years in growth hormone (GH)-deficient childhood survivors of brain tumors receiving GH replacement.
AUTHOR: Gleeson Helena K; Stoeter Rachel; Ogilvy-Stuart Amanda L; Gattamaneni H R; Brennan Bernadette M; Shalet Stephen M
CORPORATE SOURCE: Departments of Endocrinology, Pediatric Oncology and Clinical Oncology, Christie Hospital, Manchester, United Kingdom M20 4BX.
SOURCE: The Journal of clinical endocrinology and metabolism, (2003 Aug) Vol. 88, No. 8, pp. 3682-9.
Journal code: 0375362. ISSN: 0021-972X.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 14 Aug 2003
Last Updated on STN: 12 Sep 2003
Entered Medline: 11 Sep 2003

AB Final height (FH) outcome is important in survivors of childhood brain tumors. GH replacement is indicated in those found to be GH deficient (GHD). More recently, GnRH analogs (GnRHa) have been introduced to delay early or rapidly progressing puberty to allow more time for linear growth. Studies to FH are important to determine the effectiveness of growth-promoting strategies. Our aim was to assess whether evolving endocrine strategies have improved FH outcome and to determine whether GnRHa therapy has contributed auxologically. FH data were examined in 58 children (31 males and 27 females) with radiation-induced GHD who had been treated with GH. All had received a combination of cranial (CI; n = 17) or craniospinal (CSI; n = 41) irradiation with or without chemotherapy for a brain tumor. Eleven patients received GnRHa therapy. Throughout the 25 yr of the study patients came closer to achieving target height (i.e. a reduction in height loss), both those receiving CI (r = 0.5; P = 0.03) and those receiving CSI (r = 0.6; P < 0.001). The patients receiving GH therapy before 1988 compared with from 1988 onward had a similar age at irradiation [mean (+/-SD), 5.8 (3.0) vs. 6.2 (2.9) yr; P = 0.6], but experienced a more prolonged time interval from completing irradiation to starting GH [5.4 (2.4) vs. 3.3 (1.6) yr; P < 0.001]. Forward stepwise regression analysis revealed that height loss is affected by age at irradiation (P < 0.001), previous spinal irradiation (P = 0.02), chemotherapy (P < 0.001), and exposure to GnRHa therapy (P < 0.001). In the 11 patients treated with GnRHa therapy FH SD scores were improved compared with FH predictions calculated from a model derived from the patients not treated with GnRHa [-0.8 (1.6) vs. -2.4 (0.8) SD score; P < 0.001]. We have demonstrated an overall improvement in FH in children treated with GH for GHD after therapy for brain tumors over the last 25 yr. In the subset of children in whom the growth prognosis was adversely affected by early puberty, the combination of GnRHa and GH improved their prospects of achieving target height. The improved auxological outcome may reflect 1) the use of more standardized GH schedules and better dosing regimens, 2) a reduction in the time interval between finishing radiotherapy and receiving GH replacement, and 3) the use of GnRHa in addition to GH replacement in carefully selected patients.

L4 ANSWER 7 OF 24 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2003126120 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12639697
TITLE: New approaches to treatment of various cancers based on cytotoxic analogs of LHRH, somatostatin and bombesin.
AUTHOR: Schally Andrew V; Nagy Attila
CORPORATE SOURCE: Endocrine, Polypeptide, and Cancer Institute, Veterans Affairs Medical Center, New Orleans, LA 70112, USA.. nagy@tulane.edu
SOURCE: Life sciences, (2003 Apr 11) Vol. 72, No. 21, pp. 2305-20.
Ref: 67
Journal code: 0375521. ISSN: 0024-3205.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304

ENTRY DATE: Entered STN: 18 Mar 2003
Last Updated on STN: 9 Apr 2003
Entered Medline: 8 Apr 2003

AB The development of targeted cytotoxic analogs of hypothalamic peptides for the therapy of various cancers is reviewed and various oncological studies on experimental tumors are summarized. Novel therapeutic modalities for breast, prostate and ovarian cancer consist of the use of targeted cytotoxic analogs of LH-RH containing doxorubicin (DOX) or 2-pyrrolino-DOX. The same radicals have been incorporated into cytotoxic analogs of somatostatin which can be also targeted to receptors for this peptide in prostatic, mammary, ovarian, renal and lung cancers, brain tumors and their metastases. A targeted cytotoxic analog of bombesin containing 2-pyrrolino-DOX has also been synthesized and successfully tried in experimental models of prostate cancer, small cell lung carcinoma and brain tumors. The development of these new classes of peptide analogs should lead to a more effective treatment for various cancers.

L4 ANSWER 8 OF 24 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003081345 EMBASE
TITLE: [Precoccious puberty in girl with brain tumor - 14-Years observation].
PRZEDWCZESNE DOJRZEWANIE PlCIOWE U DZIEWCZYNKI W PRZEBIEGU GUZA MOZGU - 14-LETNIA OBSERWACJA.
AUTHOR: Iwanicka Z.; Glab E.
CORPORATE SOURCE: Dr. Z. Iwanicka, ul. Obroncow Poczty Gdariskiej 66/17, 52-204 Wroclaw, Poland
SOURCE: Pediatria Polska, (2003) Vol. 78, No. 1, pp. 63-67. .
Refs: 20
ISSN: 0031-3939 CODEN: PEPOA6
COUNTRY: Poland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
008 Neurology and Neurosurgery
010 Obstetrics and Gynecology
014 Radiology
037 Drug Literature Index
LANGUAGE: Polish
SUMMARY LANGUAGE: English; Polish
ENTRY DATE: Entered STN: 6 Mar 2003
Last Updated on STN: 6 Mar 2003

AB We present the influence of a GnRH analog on central precocious puberty (CPB) in a girl with hypothalamic hamartoma (HH). The first symptoms of CPP occurred after birth as irregular metrorrhagia. The diagnosis was established at the age of 2.5 years according to clinical features, MRI of the brain, and ultrasound examination of the ovaries. The very early onset of CPP and advanced bone age (9/2.5 years) suggest an inherited malformation. Therapy with Decapeptyl at 3.75 mg i.m. every 28 days was introduced. Complete regression of symptoms and hormonal abnormalities was observed. Follow-up MRI of the brain did not show progression. Neurological status in the time of observation was normal. The therapy was stoped at the age of 14 years.

L4 ANSWER 9 OF 24 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001109736 EMBASE
TITLE: Disorders of growth and puberty in children with non-tumoral hydrocephalus.
AUTHOR: Cholley F.; Trivin C.; Sainte-Rose C.; Souberbielle J.C.; Cinalli G.; Brauner R.
CORPORATE SOURCE: R. Brauner, Service d'Endocrinol. et Croissance, Hop. Necker-Enfants Malades, 149 rue de Sevres, 75743 Paris Cedex 15, France. raja.brauner@wanadoo.fr

SOURCE: Journal of Pediatric Endocrinology and Metabolism, (2001) Vol. 14, No. 3, pp. 319-327. .
Refs: 24
ISSN: 0334-018X CODEN: JPEMFT
COUNTRY: Israel
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
007 Pediatrics and Pediatric Surgery
008 Neurology and Neurosurgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Apr 2001
Last Updated on STN: 12 Apr 2001

AB Hydrocephalus may cause disorders of growth and puberty. 31 patients (25 girls) with non-tumoral hydrocephalus were seen at 8.5 ± 3.1 (SD) years for short stature (8 patients), overweight (8 patients), central early puberty (onset before 9 years, 21 patients), premature pubarche (1 patient) and/or delayed puberty (2 patients). Among the patients with short stature, 4 had meningomyelocele and one had untreated early puberty. Only 1/11 patients evaluated had growth hormone deficiency. Among the overweight patients, 5 had early puberty. The plasma leptin concentrations were positively correlated with the body mass index ($r = 0.65$, $p < 0.01$, $n = 14$). Free thyroxin, cortisol, prolactin and concomitant plasma and urinary osmolalities were normal in all cases evaluated, except one who had low free thyroxin. The 7 patients with early puberty and who were given gonadotropin releasing hormone analog for over 2 years had mean predicted adult height of -2.45 ± 1.9 SD before treatment and -2.46 ± 1.4 SD afterwards. Ventriculocisternostomy performed on 2 girls seen for delayed puberty was followed by breast development and menarche. In conclusion, in children with hydrocephalus, short stature is frequently due to meningomyelocele and rarely to GH deficiency. Central early puberty is the most frequent endocrine disorder.

L4 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:53463 CAPLUS
DOCUMENT NUMBER: 130:76610
TITLE: Assays of gonadotropin-releasing hormone receptor and the use hormone effectors in the treatment of tumors of the nervous system
INVENTOR(S): Van Groeninghen, Johannes Christianus
PATENT ASSIGNEE(S): Van Groeningen, Johannes Christianus, Germany
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9901764	A2	19990114	WO 1998-DE1902	19980703
WO 9901764	A3	19990514		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19728737	C1	19990211	DE 1997-19728737	19970704

CA 2295577	A1	19990114	CA 1998-2295577	19980703
AU 9892515	A	19990125	AU 1998-92515	19980703
EP 993613	A2	20000419	EP 1998-944968	19980703
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2006342177	A	20061221	JP 2006-217259	20060809
PRIORITY APPLN. INFO.:			DE 1997-19728737	A 19970704
			JP 1999-506130	A3 19980703
			WO 1998-DE1902	W 19980703

AB A method for recognizing and quantifying gonadotropin-releasing hormone receptors (GnRH receptors) on abnormal cells of a tumor originating in the brain, nervous system, meninges or in Kaposi's sarcoma is described. The method can be used in the diagnosis of these tumors. The use of GnRH agonists and antagonists or other ligands for GnRH receptors in the development of drugs for the treatment of these tumors is also described.

L4 ANSWER 11 OF 24 MEDLINE on STN DUPLICATE 5

ACCESSION NUMBER: 1999258039 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10326189
TITLE: Effects of puberty on bone age maturation in a girl after medulloblastoma therapy.
AUTHOR: Marx M; Schoof E; Grabenbauer G G; Beck J D; Doerr H G
CORPORATE SOURCE: Division of Paediatric Endocrinology, University of Erlangen-Nuremberg, Germany.
SOURCE: Journal of pediatric and adolescent gynecology, (1999 May) Vol. 12, No. 2, pp. 62-6.
Journal code: 9610774. ISSN: 1083-3188.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 14 Jul 1999
Last Updated on STN: 14 Jul 1999
Entered Medline: 29 Jun 1999

AB BACKGROUND: Craniospinal radiotherapy for malignant brain tumors can result in a variety of neuroendocrine disturbances, among which are the development of growth hormone deficiency and early puberty, which can markedly reduce adult height. METHODS: The authors report the case of a girl who received craniospinal radiotherapy for a medulloblastoma at the age of 3.4 years. At 9.1 years, growth hormone therapy was started, and spontaneous onset of puberty (Tanner stage B2) occurred at age 10.3 years. Interval until menarche was short, at only 0.9 years. RESULTS: Although chronologic age at appearance of Tanner stages was within the normal range, the patient showed a rapid acceleration in skeletal maturation, resulting in adult short stature. CONCLUSION: Bone age seems to be a more precise parameter for biologic maturation in some patients after craniospinal irradiation than is clinical assessment of pubertal stages. Thus, if progression of bone age and decreasing final height predictions are noted, puberty should be stopped with gonadotropin-releasing hormone analogs, even if pubertal development seems to be adequate for chronologic age, because this increases the remaining time for growth hormone treatment.

L4 ANSWER 12 OF 24 MEDLINE on STN DUPLICATE 6

ACCESSION NUMBER: 1999337640 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10407215
TITLE: Cancer chemotherapy based on targeting of cytotoxic peptide conjugates to their receptors on tumors.
AUTHOR: Schally A V; Nagy A

CORPORATE SOURCE: Section of Experimental Medicine, Department of Medicine, Tulane University School of Medicine, New Orleans, Louisiana 70112--2699, USA.
SOURCE: European journal of endocrinology / European Federation of Endocrine Societies, (1999 Jul) Vol. 141, No. 1, pp. 1-14. Ref: 102
Journal code: 9423848. ISSN: 0804-4643.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 27 Aug 1999
Last Updated on STN: 27 Aug 1999
Entered Medline: 19 Aug 1999

AB In view of non-specific toxicity of most chemotherapeutic agents against normal cells, the development of targeted chemotherapy is warranted. Efficient targeting of chemotherapeutic drugs to the cancerous area could be of great benefit for patients with advanced or metastatic tumors. Targeted cytotoxic peptide conjugates are hybrid molecules composed of a peptide carrier which binds to receptors on tumors and a cytotoxic moiety. New cytotoxic analogs of LHRH, AN-152 in which doxorubicin (DOX) is linked to [d-Lys(6)]LHRH, and AN-207 which consists of 2-pyrrolino-DOX (AN-201) coupled to the same carrier, show high-affinity binding and are much less toxic and more effective in vivo than their respective radicals in inhibiting tumor growth in LHRH receptor-positive models of human ovarian, mammary, or prostatic cancer. These results suggest that targeted cytotoxic LHRH analogs such as AN-207 could be considered for treatment of these cancers. The presence of receptors for bombesin-like peptides on a wide variety of tumors prompted us to use some of our bombesin/gastrin-releasing peptide antagonists as carrier molecules. Cytotoxic bombesin analogs, such as AN-215 containing AN-201, might find application in the treatment of small cell lung carcinoma (SCLC), and colorectal, gastric, pancreatic, mammary, and prostatic cancers. Since somatostatin receptors are found in various human neoplasms and the receptor subtypes to which octapeptide analogs bind with high affinity have been identified, we synthesized several cytotoxic somatostatin analogs including AN-162 and AN-238 containing DOX and 2-pyrrolino-DOX respectively, linked to octapeptide RC-121. Cytotoxic somatostatin analog AN-238 efficaciously inhibits growth of human breast or prostate cancers expressing somatostatin receptors-2 and -5 and can be used for receptor-targeted chemotherapy. Cytotoxic somatostatin analogs might also find applications for the therapy of human pancreatic, colorectal, and gastric cancer as well as brain tumors and non-SCLC. Cytotoxic compounds linked to analogs of hormonal peptides like LHRH, bombesin, and somatostatin that can be targeted to certain tumors possessing receptors for those peptides could be an important addition to oncological armamentarium.

L4 ANSWER 13 OF 24 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 97395596 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9251734
TITLE: Increased LH and FSH secretion after cranial irradiation in boys.
AUTHOR: Lannering B; Jansson C; Rosberg S; Albertsson-Wikland K
CORPORATE SOURCE: Department of Paediatrics, University of Goteborg, Sweden.
SOURCE: Medical and pediatric oncology, (1997 Oct) Vol. 29, No. 4, pp. 280-7.
Journal code: 7506654. ISSN: 0098-1532.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 16 Sep 1997
Last Updated on STN: 16 Sep 1997
Entered Medline: 3 Sep 1997

AB The effect of high-dose cranial- and craniospinal irradiation and chemotherapy on the gonadotropin-sex steroid axis was studied during different stages of puberty by measuring pulsatile secretion of luteinizing hormone (LH), follicle-stimulating hormone (FSH) and testosterone. The patients were thirteen boys who had been treated for malignant brain tumor residing well away from the hypothalamo-pituitary region. The median time to follow-up was 9 (1-16) years. The onset of puberty was early in the patients, median 10.5 years, compared to the average age for Swedish boys, which is at median 12.4 years. There was, before puberty, no significant difference in LH and FSH secretion between patients and a control group of normal boys. In early, mid- and late stages of puberty, however, LH and FSH secretion was increased in the patients overall, whereas testosterone secretion was maintained within the normal range in spite of signs of gonadotoxocity with small testicular volumes. These results indicate that the vulnerable parts of the gonadotropin releasing hormone (GnRH)-gonadotropin (LH, FSH)-gonadal axis are the regulatory system that determines the timing of pubertal induction and the gonads. The GnRH-LH, FSH-releasing neurons appear relatively resistant to cranial irradiation as they are able to respond with supranormal LH and FSH levels for long periods of time after treatment.

L4 ANSWER 14 OF 24 EMBASE

ACCESSION NUMBER: 97074080 EMBASE
DOCUMENT NUMBER: 1997074080
TITLE: Pituitary hyperplasia in a girl with gonadal dysgenesis and primary hypothyroidism.
AUTHOR: Riedl S.; Frisch H.
CORPORATE SOURCE: H. Frisch, Univ-Kinderklinik-Endokrinologie, Wahringer Gurtel 18-20, A-1090 Wien, Austria
SOURCE: Hormone Research, (1997) Vol. 47, No. 3, pp. 126-130. .
Refs: 25
ISSN: 0301-0163 CODEN: HRMRA3
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
005 General Pathology and Pathological Anatomy
007 Pediatrics and Pediatric Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Mar 1997
Last Updated on STN: 24 Mar 1997

AB A 16-year-old Brazilian girl presented with severe growth retardation (-6.3 SDS), obesity, delayed pubertal development, facial dysmorphia, dry skin, and borderline low intelligence (IQ 89). Endocrinological evaluation showed primary hypothyroidism (no uptake of iodine-131 of the right thyroid lobe). Basal and stimulated gonadotropins were increased and ultrasonography revealed hypoplastic ovaries. The karyotype of peripheral lymphocytes was 46,X,i(Xq). The GH response in euthyroid condition after stimulation with GHRH and insulin was diminished. MRI of the pituitary region showed a suprasellar mass (12 x 15 mm) which was removed by transsphenoidal surgery because of extension to the optic chiasm. Histological examinations revealed regular pituitary tissue with hyperplasia of TSH- and FSH-producing cells. Thyroxine treatment was adjusted and GH was given. We conclude that the suprasellar mass was the consequence of long-lasting hypothalamic overstimulation with TRH and LHRH, due to gonadal and thyroid insufficiency.

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ACCESSION NUMBER: 94334502 EMBASE
DOCUMENT NUMBER: 1994334502
TITLE: Potential for fertility with replacement of hypothalamic gonadotropin- releasing hormone in long term female survivors of cranial tumors.
AUTHOR: Hall J.E.; Martin K.A.; Whitney H.A.; Landy H.; Crowley Jr. W.F.
CORPORATE SOURCE: Reproductive Endocrine Unit, Bartlett Hall Extension-5, Massachusetts General Hospital,Boston, MA 02114, United States
SOURCE: Journal of Clinical Endocrinology and Metabolism, (1994) Vol. 79, No. 4, pp. 1166-1172. .
ISSN: 0021-972X CODEN: JCEMAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 7 Dec 1994
Last Updated on STN: 7 Dec 1994

AB Dysfunction of the hypothalamic-pituitary axis presenting as hypogonadotropic amenorrhea is a common sequelae of treatment for cranial tumors with surgery and/or radiation. We hypothesized that the site of the defect in this condition is hypothalamic, rather than pituitary, in the majority of patients. Nine women with acquired hypogonadotropic hypogonadism after treatment with transphenoidal pituitary surgery (n = 3), transphenoidal surgery plus conventional radiotherapy (XRT; n = 1), hypothalamic surgery plus XRT (n = 2), or XRT with or without noncentral nervous system surgery (n = 3) underwent assessment of endogenous pulsatile LH secretion and a standard GnRH test followed by iv administration of a physiological replacement regimen of exogenous GnRH. A total of 25 cycles were completed at doses of 75 or 100 ng/kg · bolus. Ovulation occurred in 78% of patients, with all ovulatory patients who desired fertility becoming pregnant. The hormonal responses in these cycles did not differ from the patterns of sex steroids and gonadotropins in normal women. The response to pulsatile GnRH was not influenced by GH deficiency or PRL abnormalities. Of the two patients who failed to ovulate, there was no evidence of folliculogenesis in one, whereas the second consistently developed follicles, but proved incapable of mounting a LH surge despite adequate preovulatory estradiol levels. Both patients had a history of pituitary radiation and surgery. There was no consistent relationship between the results of GnRH testing and the pattern of pulsatile LH secretion. However, the only patient who failed to achieve folliculogenesis was the only patient without a FSH response to GnRH testing and an apulsatile baseline study. Hypothalamic GnRH deficiency is the etiology of hypogonadism in the majority of patients after treatment with hypothalamic or pituitary surgery or cranial irradiation. Therefore, exogenous pulsatile GnRH represents a physiological replacement therapy that completely restores normal gonadotropin dynamics, resulting in ovulation and fertility.

L4 ANSWER 16 OF 24 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 94290554 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8019607
TITLE: [Management of female precocious puberty]. Conduite a tenir devant une precocite pubertaire feminine.
AUTHOR: Toublanc J E
CORPORATE SOURCE: Departement de pediatrie, Hopital Saint-Vincent-de-Paul,

Paris.
SOURCE: Contraception, fertilite, sexualite (1992); (1994 Mar) Vol. 22, No. 3, pp. 173-7. Ref: 24
Journal code: 9314045. ISSN: 1165-1083.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 15 Aug 1994
Last Updated on STN: 15 Aug 1994
Entered Medline: 2 Aug 1994

AB Occurrence of any pubertal sign before eight years of age defines premature sexual development but does not always mean precocious puberty (PP); one should distinguish borderline physiological situations which need only a follow-up and frankly pathological situations which need very precise investigations and suitable treatment. The first situations are premature thelarche, pubarche and menarche in which the height and bone maturation, pelvic ultrasonography (US) are normal for age, avoiding hormonal investigations. Conversely in the second situation, the bone age is more advanced than the height age and the pelvic US displays ovarian activity and uterine development. The next step is the characterization of the level of the mechanism of puberty: hypothalamohypophysal or ovarian: in the first case gonadotropin levels are elevated after GnRH infusion, in the second case, depressed. The aetiological diagnosis are in true PP: brain tumors malformations or hamartoma even if negative idiopathic. At ovarian level: ovarian tumors or McCune Albright syndrome or recurrent cysts. The first etiology leads to use GnRH analog in the second the treatment is more delicate.

L4 ANSWER 17 OF 24 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1993:370338 BIOSIS
DOCUMENT NUMBER: PREV199396056013
TITLE: Induction of testicular growth and spermatogenesis by pulsatile, intravenous administration of gonadotrophin-releasing hormone in patients with hypogonadotrophic hypogonadism.
AUTHOR(S): Delemarre-Van De Waal, Henriette
CORPORATE SOURCE: Dep. Pediatrics, Free Univ. Hosp., PO Box 7057, 1007 MB, Amsterdam, Netherlands Antilles
SOURCE: Clinical Endocrinology, (1993) Vol. 38, No. 5, pp. 473-480.
CODEN: CLECAP. ISSN: 0300-0664.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 1993
Last Updated on STN: 6 Aug 1993

AB OBJECTIVE: To induce testicular growth including spermatogenesis, 38 patients with hypogonadotropic hypogonadism were treated with long-term pulsatile GnRH administration. Patients: The group of patients comprised 17 individuals with idiopathic hypogonadotrophic hypogonadism, 11 with Kallmann's syndrome, four with multiple pituitary hormone deficiencies and six with a secondary hypogonadotrophic hypogonadism due to surgical removal of a brain tumour. Thirteen patients (seven with idiopathic hypogonadotrophic hypogonadism and six with Kalmann's syndrome) had undescended testes, of whom six had undergone surgery on both testes and four on one testis. Sixteen of the 17 had previously received androgen therapy and six others had received gonadotrophin treatment, of whom three had long-term treatment to induce testicular development, without success. TREATMENT: GnRH was administered intravenously in a dose of 2-20 mu-g per pulse every 90 minutes. After GnRH discontinuation, hCG

treatment was instituted, 1500-3000 IU (i.m.) twice weekly. RESULTS: During treatment plasma levels of LH, FSH and testosterone increased. In 35 out of the 38 patients plasma testosterone levels increased into the normal adult range. In all patients testicular volume increased. Mean pretreatment testicular volume per patient group ranged from 2.4 to 4.8 ml and increased to 11.5-18.1 ml by the end of treatment. There wasa a significant difference in the achieved testicular volume between the patients with Kallmann's syndrome and the brain tumor patients. GnRH treatment mean lasted between 46 and 75 weeks in the different groups. On hCG therapy, testicular development was either maintained or improved. Semen analysis revealed the presence of spermatogenesis in 31 out of the 38 patients (26 patients already on GnRH, and in another five patients in hCG therapy). All three patients pretreated with gonadotrophins as well as three patients with bilateral testicular surgery developed a detectable sperm count. In 19 adolescent patients with growth potential, an adequate height velocity was observed during GnRH treatment. CONCLUSIONS: GnRH is a feasible way to induce testicular growth as well as spermatogenesis in hypogonadotrophic male patients, even in patients in whom gonadotrophin treatment has failed. After GnRH treatment, hCG alone can maintain or even improve testicular development, including spermatogenesis. GnRH treatment may also induce a physiological growth spurt in hypogonadotrophic adolescents.

L4 ANSWER 18 OF 24 EMBASE

ACCESSION NUMBER: 91111439 EMBASE
DOCUMENT NUMBER: 1991111439
TITLE: Treatment of central precocious puberty with LHRH analogue.
AUTHOR: Canete Estrada R.; Garcia Hortelano M.T.; Buron Romero A.; Romanos Lezcano A.
CORPORATE SOURCE: Departamento de Pediatria, Hospital Regional 'Reina Sofia', Avda. Menedez Pidal, s/n, 14004 Cordoba, Spain
SOURCE: Revista Espanola de Pediatria, (1991) Vol. 46, No. 277, pp. 19-24. .
ISSN: 0034-947X CODEN: REPEAW
COUNTRY: Spain
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
007 Pediatrics and Pediatric Surgery
037 Drug Literature Index
LANGUAGE: Spanish
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Dec 1991
Last Updated on STN: 16 Dec 1991
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L4 ANSWER 19 OF 24 EMBASE

ACCESSION NUMBER: 90280394 EMBASE
DOCUMENT NUMBER: 1990280394
TITLE: [PPubertas praecos in girls - Results of treatment with LHRH-analogues. With 2 figures].
ECHTE FRUHREIFE BEI MADCHEN. EINE THERAPIE MIT LHRH -ANALOGEN. MIT 2 ABBILDUNGEN.
AUTHOR: Wasikowa R.; Iwanicka Z.; Pellar J.; Hirowska I.; Barg E.
CORPORATE SOURCE: I. Kinderklinik der Medizinischen Akademie, ul. Wronskiego 13, 50-376 Wroclaw/VR, Poland
SOURCE: Kinderarztliche Praxis, (1990) Vol. 58, No. 7, pp. 335-340. .
ISSN: 0023-1495 CODEN: KIPRAM
COUNTRY: Germany

DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
007 Pediatrics and Pediatric Surgery
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 1991
Last Updated on STN: 13 Dec 1991
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L4 ANSWER 20 OF 24 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 90315384 EMBASE
DOCUMENT NUMBER: 1990315384
TITLE: The natural course of growth hormone-secreting pituitary adenomas after surgery alone: Clinical significance of the growth hormone response to thyrotropin-releasing hormone and luteinizing hormone-releasing hormone.
AUTHOR: Mukada K.
CORPORATE SOURCE: Department of Neurosurgery, Hiroshima University School of Medicine, 1-2-3 Kasumi, Minami-ku, Hiroshima 734, Japan
SOURCE: Neurologia Medico-Chirurgica, (1990) Vol. 30, No. 4, pp. 251-257. .
ISSN: 0387-2572 CODEN: NMCHBN
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
008 Neurology and Neurosurgery
009 Surgery
016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 1991
Last Updated on STN: 13 Dec 1991

AB The clinical significance of abnormal growth hormone (GH) secretion in response to thyrotropin-releasing hormone (TRH) and luteinizing hormone-releasing hormone (LHRH) was studied in 52 patients with acromegaly due to GH secreting pituitary adenomas treated by trans-sphenoidal microsurgery. The mean period of postoperative follow-up was 4.1 years. In 27 of the 36 patients who had abnormal GH responses to TRH or LHRH before surgery, basal GH levels normalized and abnormal GH responses disappeared immediately after surgery. Among the remaining nine patients, four had normal basal GH levels with abnormal GH responses and five showed persistently abnormal basal GH levels as well as abnormal GH responses. Recurrence requiring retreatment was not observed during follow-up in any of the 31 patients with normal postoperative basal GH levels, regardless of the GH response to TRH or LHRH. All five patients with abnormal basal GH and abnormal GH responses required additional treatment. Among the patients who underwent long-term postoperative TRH and LHRH testing, abnormal GH responses reappeared in three of 19 whose abnormal responses had disappeared immediately after surgery. The abnormal response disappeared spontaneously in two of three patients who had abnormal responses immediately after surgery. In four patients with both abnormal GH responses and abnormal basal GH levels immediately after surgery, abnormal GH responses persisted throughout the follow-up period. In addition, the abnormal GH responses appeared in two of 14 patients who had been nonresponsive before surgery. These results indicate that the postoperative GH response to TRH or to LHRH was not significantly related to the outcome. Therefore, additional or prophylactic treatment should not be administered solely on the basis of the persistence of abnormal GH response. The most reliable

predictor of long-term outcome appears to be the basal GH level immediately after surgery.

L4 ANSWER 21 OF 24 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 9

ACCESSION NUMBER: 89120947 EMBASE
DOCUMENT NUMBER: 1989120947
TITLE: Ovarian function following chemotherapy for childhood brain tumours.
AUTHOR: Clayton P.E.; Shalet S.M.; Price D.A.; Morris Jones P.H.
CORPORATE SOURCE: Department of Child Health, Royal Manchester Children's Hospital, Manchester, United Kingdom
SOURCE: Medical and Pediatric Oncology, (1989) Vol. 17, No. 2, pp. 92-96. .
ISSN: 0098-1532 CODEN: MPONDB
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 003 Endocrinology
007 Pediatrics and Pediatric Surgery
008 Neurology and Neurosurgery
010 Obstetrics and Gynecology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Dec 1991
Last Updated on STN: 12 Dec 1991

AB Pubertal development, basal gonadotrophin, and oestradiol levels were assessed in 21 girls who had received neuroaxis irradiation for a brain tumour followed by adjuvant chemotherapy with carmustine (BCNU) or lomustine (CCNU) and procarbazine. Thirteen received chemotherapy before the age of 11 years. Ten remained prepubertal at their last assessment, nine of whom showed biochemical evidence of primary ovarian failure. The remaining three were pubertal or adult, and although basal follicle-stimulating hormone (FSH) and luteinising hormone (LH) levels were normal, all had shown abnormalities of gonadotrophin secretion previously. Eight girls received chemotherapy after 11 years of age. Only three girls exhibited an elevated basal FSH level or exaggerated FSH response to GnRH. Elevated basal FSH values had been noted previously in two of the other five girls. All girls entered or progressed through puberty spontaneously. Seven experienced menarche at an appropriate age. However in four, gonadotrophin levels, which had been elevated, were now within the normal range. In two, menses had continued throughout with normal midfollicular oestradiol levels, whilst the other two developed secondary amenorrhoea associated with radiation-induced gonadotrophin deficiency. The majority of girls showed evidence of primary ovarian dysfunction. This did not prejudice pubertal development or the timing of menarche. Ovarian function may return to normal in the years after treatment, indicating a potential for fertility.

L4 ANSWER 22 OF 24 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 86140629 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2936759
TITLE: Long term treatment of male and female precocious puberty by periodic administration of a long-acting preparation of D-Trp6-luteinizing hormone -releasing hormone microcapsules.
AUTHOR: Roger M; Chaussain J L; Berlier P; Bost M; Canlorbe P; Colle M; Francois R; Garandeau P; Lahlou N; Morel Y; +
SOURCE: The Journal of clinical endocrinology and metabolism, (1986 Apr) Vol. 62, No. 4, pp. 670-7.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198604
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 21 Mar 1990
Entered Medline: 11 Apr 1986

AB The efficacy and safety of a delayed release formulation of the LHRH agonist D-Trp6-LHRH (LHRH-A; im microcapsules) were tested in 16 girls, 0.9-8.8 yr old, and 10 boys, 2.0-10.5 yr old, with precocious puberty. All children had advanced bone age, breast or testis enlargement, and a pubertal LH response to LHRH. Precocious puberty was idiopathic in 19 subjects and secondary to a brain tumor or other central nervous system abnormality in 7. Nine girls and 6 boys had been previously treated unsuccessfully with medroxyprogesterone and/or cyproterone acetate. The microcapsules were made of 2% LHRH-A dispersed in a biocompatible biodegradable polymeric matrix of DL-lactide-coglycolide. Sixty micrograms of LHRH-A/kg BW were given im on days 1 and 21 and thereafter every 4 weeks for 10-27 months. Plasma LHRH-A levels were measured in 13 children by means of a specific RIA. On days 3, 7, 14, and 21, mean concentrations (+/- SEM) were 295 +/- 44, 218 +/- 31, 215 +/- 45, and 224 +/- 39 pg/ml, respectively. In girls, breast enlargement disappeared, and mean uterus size decreased from 44.4 +/- 2.5 to 38.1 +/- 3.1 mm (mean +/- SEM; P less than 0.02) within 6 months. Mean ovary length decreased from 23.0 +/- 1.5 to 16.2 +/- 1.5 mm (P less than 0.01). In boys, mean testis volume decreased from 8.1 +/- 1.2 to 6.7 +/- 1.2 ml (P less than 0.02) within 6 months. In both sexes, growth velocity decreased significantly, and bone maturation was generally reduced. Plasma levels of estradiol or testosterone and FSH levels decreased significantly within 3 weeks. The LH response to LHRH was reduced to normal prepubertal values after 7 weeks. No secondary clinical or biochemical escape occurred. In 1 boy, all biological features of puberty recurred within 1 month after omission of the fifth injection. No side-effects occurred, except for transient vaginal bleeding in girls after the first or second injection. No antibodies to LHRH-A were detected in the patients' sera. This study demonstrates the ability of a delayed release formulation of LHRH-A to achieve stable levels of the drug in plasma for at least 21 days after a single im injection and to suppress pituitary and gonadal secretion and pituitary response to LHRH for as long as 2 yr after therapy. This treatment appears to be more efficient in treating both clinical and biochemical abnormalities than does treatment with inhibitory steroids. Additionally, the method of administration is more practical and ensures better patient compliance.

L4 ANSWER 23 OF 24 EMBASE

ACCESSION NUMBER: 85196208 EMBASE
DOCUMENT NUMBER: 1985196208
TITLE: Treatment of true precocious puberty with a potent luteinizing hormone-releasing factor agonist: Effect on growth, sexual maturation, pelvic sonography, and the hypothalamic-pituitary-gonadal axis.
AUTHOR: Styne D.M.; Harris D.A.; Egli C.A.; et al.
CORPORATE SOURCE: Department of Pediatrics, University of California San Francisco, CA 94143, United States
SOURCE: Journal of Clinical Endocrinology and Metabolism, (1985) Vol. 61, No. 1, pp. 142-151. .
CODEN: JCEMAZ
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
003 Endocrinology
030 Pharmacology

008 Neurology and Neurosurgery
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 10 Dec 1991

AB We used the LHRH agonist D-Trp6-Pro6-N-ethylamide LHRH (LHRH-A) to treat 19 children (12 girls and 7 boys) with true precocious puberty. Fourteen patients had idiopathic true precocious puberty, 4 had a hamartoma of the tuber cinereum, and 1 had a hypothalamic astrocytoma. Basal gonadotropin secretion and responses to native LHRH decreased within 1 week of initiation LHRH-A therapy, and sex steroid secretion decreased within 2 weeks to or within the prepubertal range. Ultrasonographic evaluation of the uterus indicated a postmenarchal size and shape in all 11 girls studied before treatment, which reverted to prepubertal size and configuration in 5 girls during LHRH-A therapy. The enlarged ovaries decreased in size and the multiple ovarian follicular cysts regressed. Sexual characteristics ceased advancing or reverted toward the prepubertal state in all patients receiving therapy for 6-36 months. All 5 girls with menarche before therapy had no further menses. Three girls had hot flashes after LHRH-A-induced reduction of the plasma estradiol concentration. Height velocity, SDs above the mean height velocity for age, and SDs above the mean height for age decreased during LHRH -A therapy; the velocity of skeletal maturation decreased after 12 months of LHRH-A therapy and was sustained during continued therapy over 18-36 months. In 4 patients, a subnormal growth rate (<4.5 cm/yr) occurred during LHRH-A therapy. Six patients had cutaneous reactions of LHRH-A, but no demonstrable circulating antibodies to LHRH-A. In 2 patients in whom LHRH-A therapy was discontinued because of skin reactions precocious sexual maturation resumed at the previous rate for the ensuing 6-12 months; subsequently, they were desensitized to LHRH-A, and during a second course of therapy, their secondary sexual development and sex steroid levels again quickly decreased. LHRH-A proved an effective and safe treatment for true precocious puberty in boys as well as girls with central precocious puberty whether of the idiopathic type or secondary to a hamartoma of the tuber cinereum or a hypothalamic neoplasm.

L4 ANSWER 24 OF 24 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1982:297494 BIOSIS
DOCUMENT NUMBER: PREV198274069974; BA74:69974
TITLE: EFFECTS OF CRANIAL RADIATION ON HYPOTHALAMIC ADENO HYPOPHYSEAL FUNCTION ABNORMAL GROWTH HORMONE SECRETORY DYNAMICS.
AUTHOR(S): CHROUSOS G P [Reprint author]; POPLACK D; BROWN T; O'NEILL D; SCHWADE J; BERCU B B
CORPORATE SOURCE: NATL INST HEALTH, BLDG 10, ROOM 13N260, BETHESDA, MD 20205, USA
SOURCE: Journal of Clinical Endocrinology and Metabolism, (1982) Vol. 54, No. 6, pp. 1135-1139.
CODEN: JCEMAZ. ISSN: 0021-972X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Cranial x-radiation is commonly used both as a treatment for brain tumors and for preventive CNS therapy in acute lymphoblastic leukemia. The function of the hypothalamic-adenohypophyseal unit was tested in 2 groups of rhesus monkeys before and at periodic intervals after the administration of 2400 and 4000 rad cranial radiation. This therapy was given in 10 fractions over a 2 wk period. Plasma TSH, basally and after TRH administration, and lutropin and FSH, before and after gonadotropin-releasing hormone stimulation, were normal up to 1 yr after radiation. Plasma GH [growth hormone] at the basal state and after arginine and L-dopa stimulation was

also normal. An insulin tolerance test, however, demonstrated a blunted GH response at a dose (0.1 U/kg) that caused brisk stimulation of GH secretion in normal control monkeys. A larger dose of insulin (0.2 U/kg) resulted in ample secretion of GH in these animals, suggesting decreased hypothalamic sensitivity to insulin in treated animals. The measurement of GH every 20 min for 24 h in animals treated with 4000 rad showed a dramatically altered secretory pattern of GH 1 yr after radiation. GH secretory spikes were markedly decreased in both frequency and amplitude, suggesting a reduction in the normal daily production of GH.